



**Armed Forces College of
Medicine
AFCM**



Diuretics (1)

By

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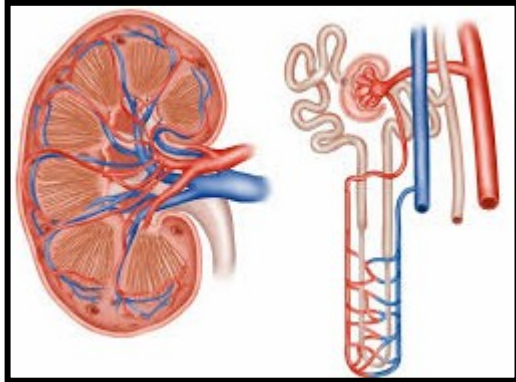
INTENDED LEARNING OBJECTIVES (ILO)



By the end of this lecture the student will be able to:

1. Identify the site of action of diuretics
2. Identify different members of diuretics
3. Explain the mechanism of action and adverse effects of different diuretics

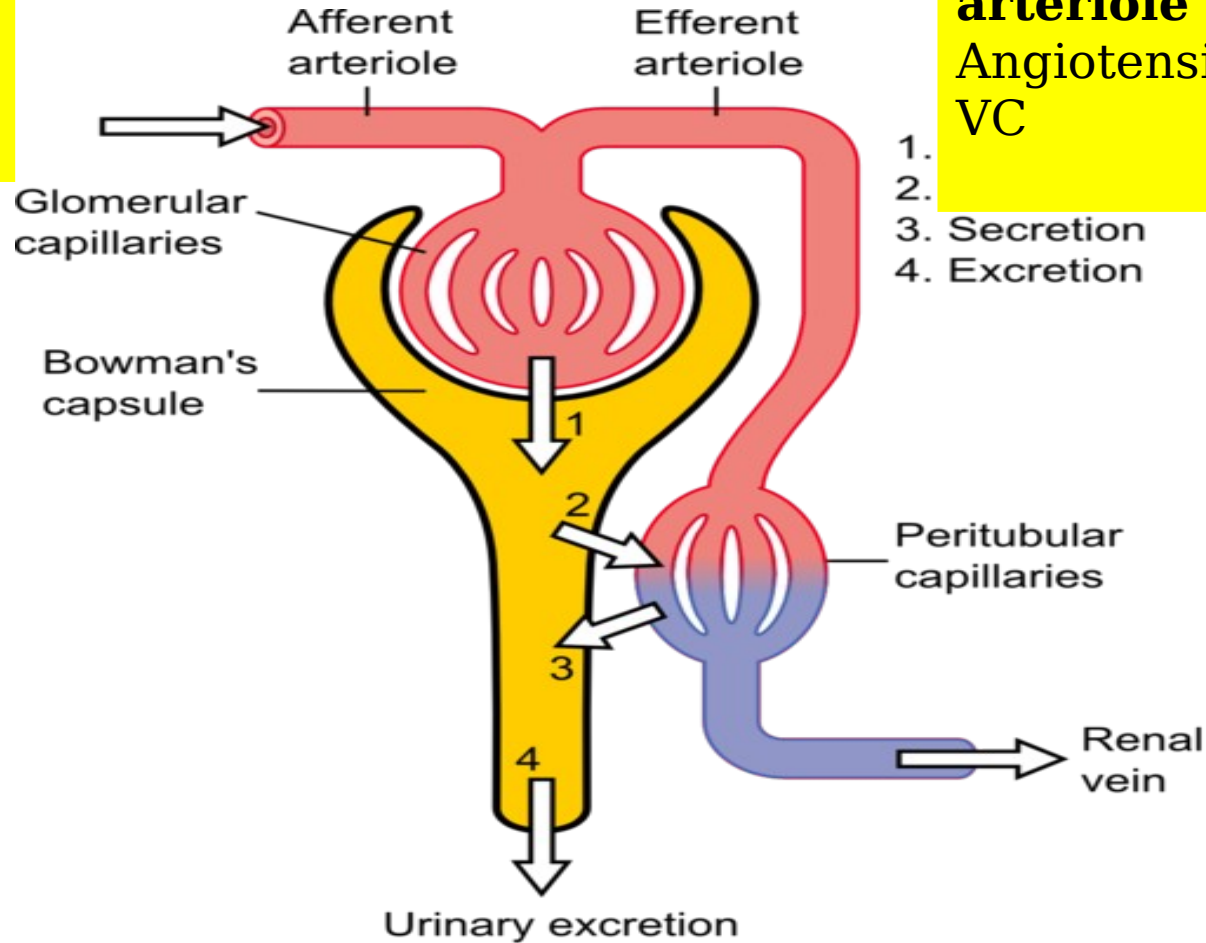




DIURETICS

Afferent arteriole
PG → **VD**

Efferent arteriole
Angiotensin II → **VC**



Maintenance of Glomerular Filtration in Hypoperfusion States

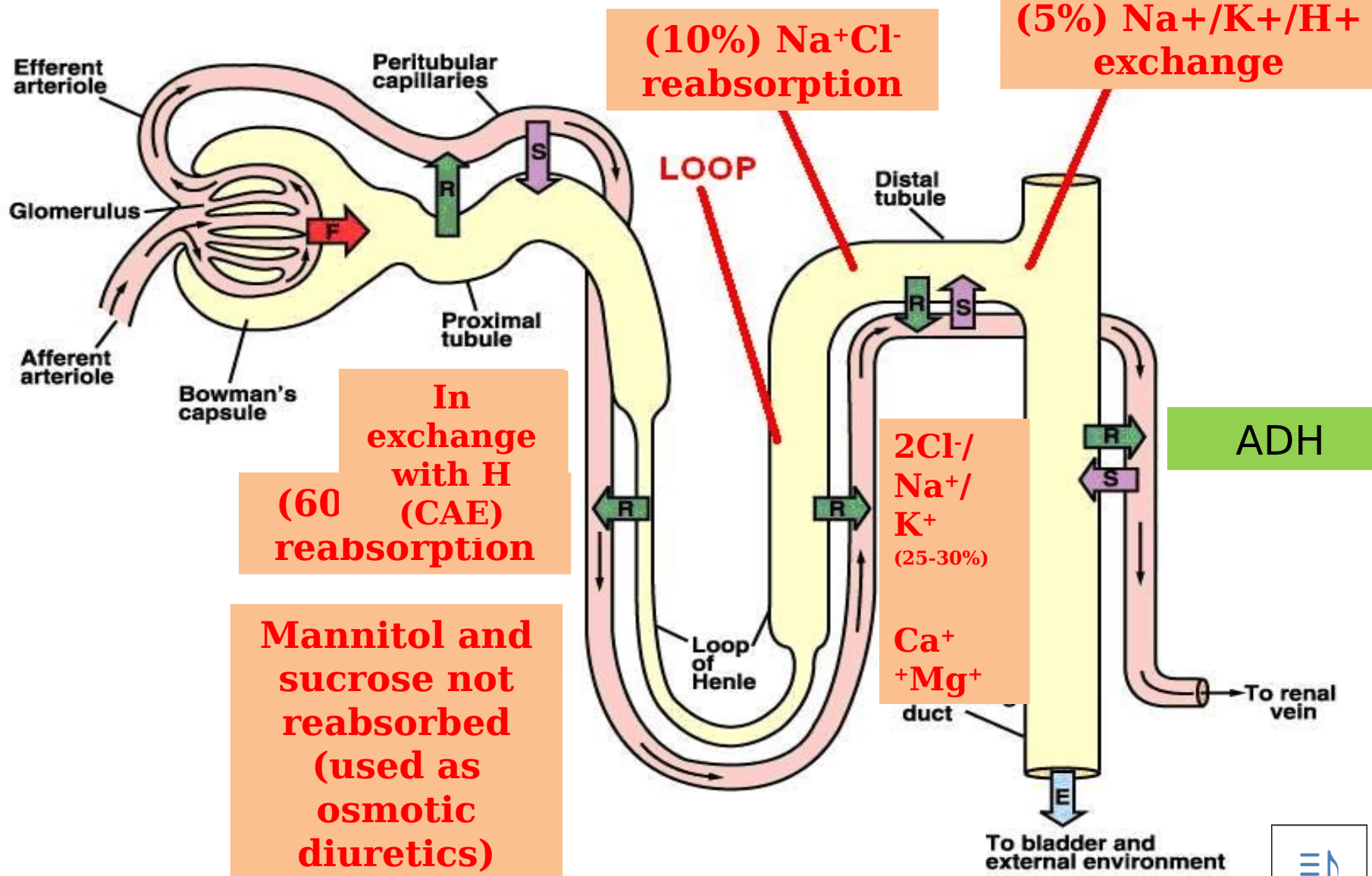
In renal hypoperfusion, glomerular pressure is $\uparrow$ to maintain GFR through: $\uparrow$ Ag II $\rightarrow$ VC of efferent arteriole & $\uparrow$ PG $\rightarrow$ VD of afferent arteriole $\rightarrow$ $\uparrow$ blood flow



- In **renal hypoperfusion** states (hypovolemia, diuretic therapy, heart failure), administration of **ACEIs** (→ inhibit efferent VC) or administration of the PG synthesis inhibitors **NSAIDs** (→ inhibit afferent VD) causes marked reduction in glomerular filtration → acute renal failure.



Transport of water and electrolytes through the nephron



Medullary hypertonicity:

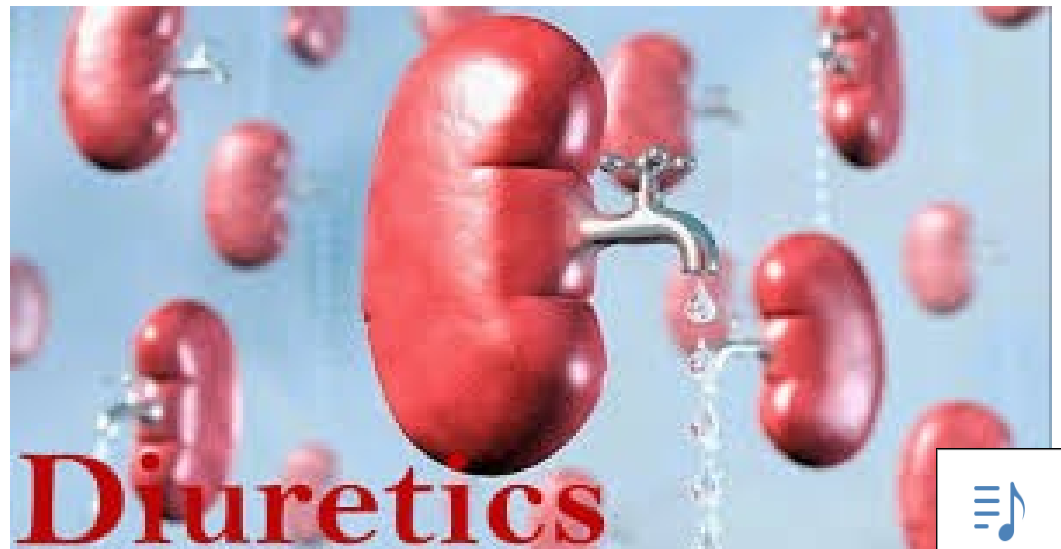
is created by active reabsorption of Na^+ coupled with passive transport of urea at this segment. It provides osmotic driving forces for water reabsorption from collecting tubules under the effect of ADH to conserve body water & concentrate urine.

Renal PG interfere with medullary hypertonicity by inhibiting Na reabsorption leading to diuresis



Diuretics

Diuretics are drugs that cause a net loss of sodium and water from the body through the kidney resulting in contraction of the extracellular fluid.

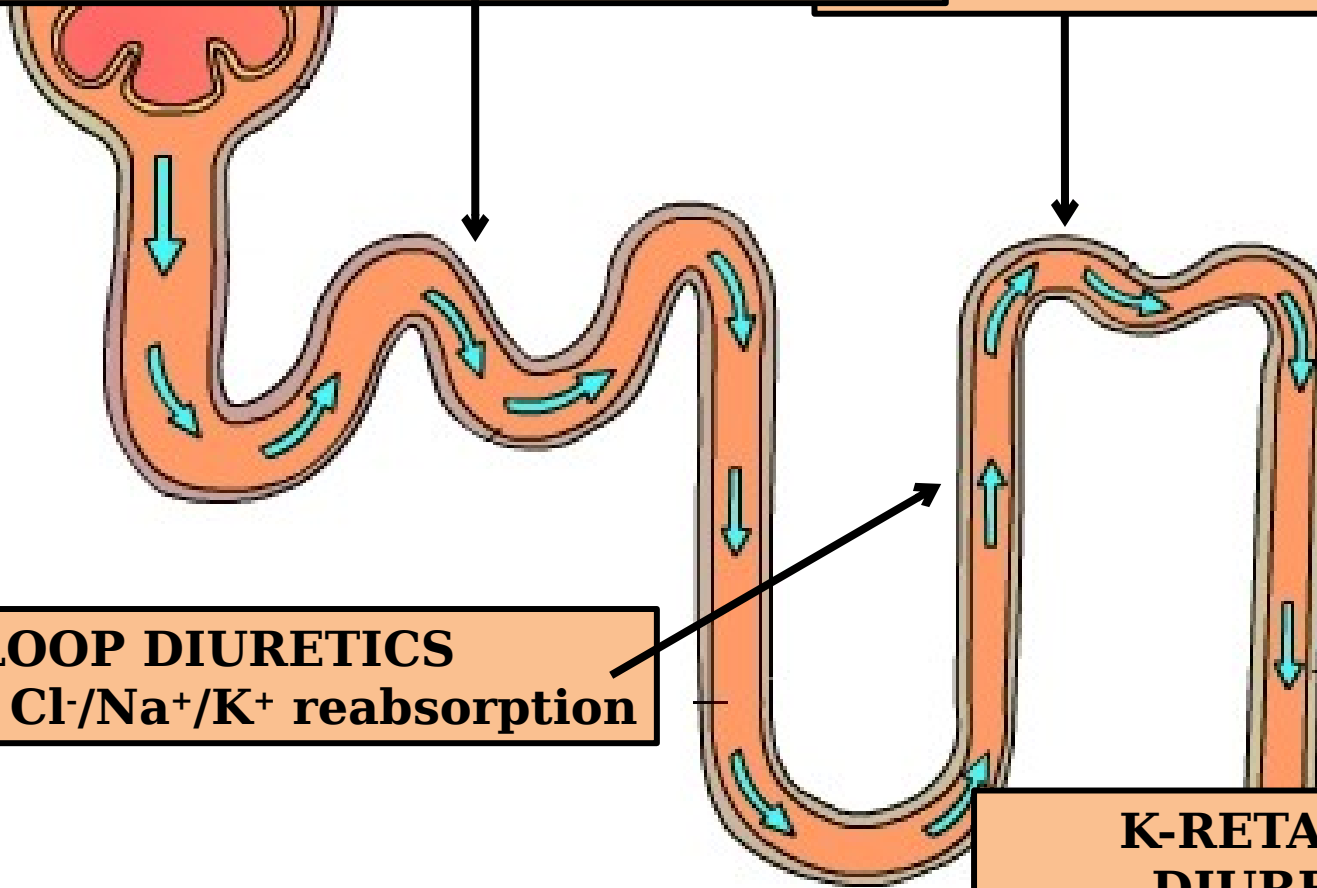


Osmotic diuretics
Mannitol

DIURETICS

Carbonic anhydrase inhibitors
inhibition of NaHCO_3 reabsorption

THIAZIDE DIURETICS
inhibit active NaCl reabsorption



LOOP DIURETICS
Block 2 $\text{Cl}^-/\text{Na}^+/\text{K}^+$ reabsorption

K-RETAINING
DIURETICS
Inhibit Na^+
reabsorption
 K^+ & H^+ excretion



Diuretic	Site of action
• Carbonic anhydrase Inhibitors	Proximal tubule
• Osmotic diuretics	Proximal tubule & loop of Henle
• Loop diuretics	Loop of Henle
• Thiazides	Early Distal tubule
• Amiloride • Triamterene • Spironolactone	Distal tubule and collecting duct



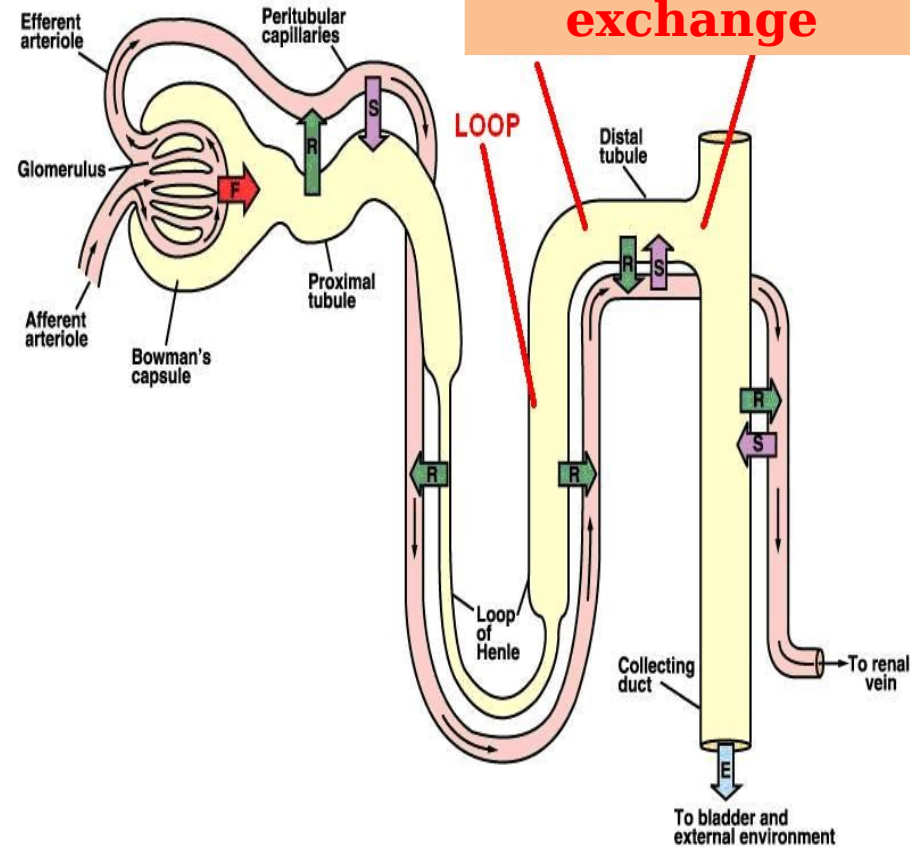
General principles in diuretic therapy

Aldosterone

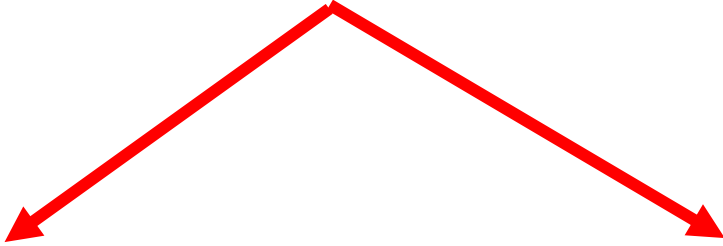
Na⁺/K⁺/H⁺ exchange

Diuretics interfering with reabsorption of Na⁺ at earlier (more proximal) sites lead to enhanced Na⁺ reabsorption in exchange with K⁺ & H⁺ at distal tubule (aldosterone-dependent Na⁺/K⁺/H⁺ exchange site)

→ hypokalemia and alkalosis.



Diuretics



A. K^+ -losing diuretics

- Loop diuretics.
- Thiazides.
- Osmotic diuretics.
- Carbonic anhydrase inhibitors.

B. K^+ -sparing diuretics

- Spironolactone
- Amiloride
- triamterene.



General principles in diuretic therapy

Diuretics act by different mechanisms and at different sites along the nephron. Thus, they have a synergistic effect if they are combined.



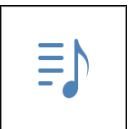
General principles in diuretic therapy

All diuretics (except spironolactone) have to reach their site of action in the lumen of the nephron, by organic acid or organic base secretory systems .

Therefore, any defect in delivery of diuretics to their sites of action (e.g. in renal impairment) will result in diminished diuretic response.



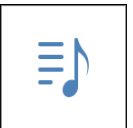
Diuretic	Route of access to site of action
• Carbonic anhydrase Inhibitors	Organic acid secretion
• Osmotic diuretics	Glomerular filtration
• Loop diuretics	Organic acid secretion
• Thiazides	Organic acid secretion
• Amiloride	Organic base secretion
• Triamterene	Organic base secretion
• Spironolactone	Peritubular circulation



Lecture quiz

- Which of the following diuretics is associated with hyperkalemia?

- A. Thiazides
- B. Loop diuretics
- C. Osmotic diuretics
- D. Carbonic anhydrase inhibitors
- E. Spironolactone



SUGGESTED TEXTBOOKS



1. Whalen, K., Finkel, R., & Panavelil, T. A. (2018) Lippincott's Illustrated Reviews: Pharmacology (7th edition.). Philadelphia: Wolters Kluwer
2. Katzung BG, Trevor AJ. (2018). Basic & Clinical Pharmacology (14th edition) New York: McGraw-Hill Medical.





Thank You